"DESIGN AND DEVELOPMENT OF SOLID-LIPID NANOPARTICLES (SLN) BASED TOPICAL GEL"

SYNOPSIS

SUBMITTED FOR REGISTRATION OF

THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN THE SUBJECT

PHARMACEUTICAL SCIENCES

At

SARDAR PATEL UNIVERSITY, BALAGHAT (M.P.)

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2019-20

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1. INTRODUCTION

1. Introduction

Solid lipid nanoparticles (SLN) introduced in 1991 represent an alternative carrier system to tradition colloidal carriers such as - emulsions, liposomes and polymeric micro – and nanoparticles. Nanoparticles made from solid lipids are attracting major attention as novel colloidal drug carrier for intravenous applications as they have been proposed as an alternative particulate carrier system. SLN are sub-micron colloidal carriers ranging from 50 to 1000 nm, which are composed of physiological lipid, dispersed in water or in aqueous surfactant solution. SLN offer unique properties such as small size, large surface area, high drug loading and the interaction of phases at the interface and are attractive for their potential to improve performance of pharmaceuticals. (Sathali AH, 2011).

Solid lipid nanoparticles (SLNs) are considered to be the most effective lipid based colloidal carriers, introduced in early nineties. This is the one of the most popular approaches to improve the oral bioavailability of the poorly water soluble drugs. SLNs are in the submicron size range of 50-1000 nm and are composed of physiologically tolerated lipid components which are in solid state at room temperature. SLNs combine all the advantages of polymeric nanoparticles, fat emulsions and liposomes. (Sathali AH, 2011).

1.1 Advantages of SLN (Sathali AH, 2011)

- Control and / or target drug release.
- Excellent biocompatibility5.
- Improve stability of pharmaceuticals4.
- High and enhanced drug content.
- Easy to scale up and sterilize.
- Better control over release kinetics of encapsulated compounds.
- Enhanced bioavailability of entrapped bioactive compounds.
- Chemical protection of labile incorporated compounds.
- Much easier to manufacture than biopolymeric nanoparticles.
- No special solvent required.
- Conventional emulsion manufacturing methods applicable.

- Raw materials essential the same as in emulsions.
- Very high long-term stability.
- Application versatility.
- Can be subjected to commercial sterilization procedures.

1.2 Disadvantages of SLN (Sathali AH, 2011)

- Particle growth.
- Unpredictable gelation tendency.
- Unexpected dynamics of polymeric transitions.

1.3 Aims of solid lipid nanoparticles (Sathali AH, 2011)

- Possibility of controlled drug release5.
- Increased drug stability.
- High drug pay load5.
- No bio-toxicity of the carrier.
- Avoidance of organic solvents.
- Incorporation of lipophilic and hydrophilic drugs.

1.4 Challenges for formulation and delivery: (Verma S, 2016)

Problems frequently occurring with many drugs are:

- Poor solubility
- Insufficient in vitro stability (shelf life)
- too low bioavailability
- Too short in vivo stability (half-life)
- Strong side effect
- need for targeted delivery
- Regulatory issues/hurdles
- Lack of large scale production

1.5 Methods of preparation: (Verma S, 2016)

- High pressure homogenization
    - Hot homogenization
    - Cold homogenization

- Ultrasonication/high speed homogenization
    - Probe ultrasonication
    - Bath ultrasonication
- Solvent evaporation method
- Solvent emulsification-evaporation method
- Supercritical fluid method
- Microemulsion based method
- Spray drying method
- Double emulsion method
- Precipitation technique
- Film-ultrasound dispersion

1.6 Evaluation of SLN:- (Sarangi MK, 2016)

- Measurement of particle size and zeta potential
- Static light scattering/Fraunhofer diffraction
- Nuclear magnetic resonance (NMR)
- Electron microscopy
- X-ray diffraction (X-ray powder diffraction)
- Differential Scanning Calorimetry (DSC)
- drug content
- *in vitro* drug release

• 2. LITERATURE REVIEW

2.1 Koteshwara BS *et al* (2017) was studied the Solid lipid nanoparticles using glyceryl monostearate by solvent emulsification method followed by probe sonication. Irbesartan loaded SLNs were characterized and optimized by parameters like particle size, zeta potential, surface morphology entrapment efficiency and *in vitro* release. The optimized formulation was then further evaluated for the pharmacokinetic studies in Wistar rats. Irbesartan-loaded SLN of particle size 523.7 nm and 73.8% entrapment efficiency showed good bioavailability in Wistar rats and also showed optimum stability in the studies.

2.2 Kesharwani R *et al* (2016) was studied solid lipid nanoparticle (SLN) based topical gel of non- steroidal anti-inflammatory drug (NSAID) etoricoxib for the treatment of arthritis which would attenuate the gastrointestinal related toxicities associated with oral administration. SLN was formulated by melt emulsification and solidification at low temperature method using stearic acid & tween 80. All the formulation was subjected to particle size, particle size distribution, zeta potential, scanning electron microscopy, crystallinity study by DSC and in-vitro release studies. It has been observed that, the high lipid concentration containing formulation have higher entrapment as compare to other two formulation. The SLN- dispersion shows 70.766% entrapment & zeta potential of the formulation was -25.6 which indicates the stability of formulation. The In Vitro drug release rate of gel was evaluated using Modified franz diffusion cell containing dialysis membrane with phosphate buffer pH 7.4 as the receptor medium. The in-vitro release was carried out in comparison with a carbopol gel & hydroxypropylmethylcellulose (HPMC) gel.

2.3 Nair R *et al* (2011) was studied the Solid lipid nanoparticles (SLN) of hydrophilic dug isoniazid (INH), a first line antubericular drug are developed and the entrapment efficiency of drug in the SLN has been improved. The poor incorporation of water soluble drugs is the problem associated with the incorporation of hydrophilic drugs in to SLN. The SLNs were prepared by ethanol injection method using tristearin and phospholipon 80 H using 32 factorial design.

3. AIM AND OBJECTIVE

3.1 Aim

To Design and develop Solid-Lipid Nanoparticles (SLN) Based Topical Gel

3.2 Objective

1. To provide prolonged and constant therapeutic effect.
2. To reduce the dosing frequency and therefore improve the patient compliance
3. To Decrease in toxicity while maintaining therapeutic effects.
4. To provide controlled, sustained and targeted delivery of the drug.
5. Development of safe medicine.

4. PLAN OF WORK

4.1. Literature survey

4.2. Procurement of Drugs and Excipients

4.3. Preformulation study

4.4. Formulation of SLN by melt emulsification method.

4.6. Evaluation of SLN

a) Measurement of particle size and zeta potential

b) Static light scattering/Fraunhofer diffraction

c) Nuclear magnetic resonance (NMR)

d) Electron microscopy

e) X-ray diffraction (X-ray powder diffraction)

f) Differential Scanning Calorimetry (DSC)

g) drug content

h) *in vitro* drug release

4.7 Results and Discussion

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